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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07C 51/47, 51/48	A3	(11) International Publication Number: WO 98/15518 (43) International Publication Date: 16 April 1998 (16.04.98)
(21) International Application Number: PCT/US97/17774 (22) International Filing Date: 2 October 1997 (02.10.97) (30) Priority Data: 119,389 9 October 1996 (09.10.96) IL (71) Applicant (for all designated States except US): CARGILL INCORPORATED [US/US]; 15407 McGinty Road West, Wayzata, MN 55391-2399 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): EYAL, Aharon, Meir [IL/IL]; 32 Baitar Street, 93380 Jerusalem (IL). ELANKO-VAN, Ponnampalam [US/US]; 2365 Club Meridian Drive, Okemos, MI 48864 (US). (74) Agents: GALLOWAY, Peter, D.; Ladas & Parry, 26 West 61st Street, New York, NY 10023 (US) et al.		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 25 June 1998 (25.06.98)

(54) Title: A PROCESS FOR THE RECOVERY OF LACTIC ACID FROM AQUEOUS LACTATE SALT SOLUTIONS, INVOLVING THE USE OF ION EXCHANGERS**(57) Abstract**

The invention provides a process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of: contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from the cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from the aqueous solution are bound by the cation exchanger; reacting the cations carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cation of the salt; and recovering lactic acid from the lactic acid-containing acidulated aqueous solution by methods known per se.

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AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/17774

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C51/47 C07C51/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 2 674 848 A (SOCIETE ANGEVINE DE BIOTECHNOLOGIE BIOPROX, FR) 9 October 1992 see page 1, line 1 - page 2, line 17 see example 2 ---	1,3-6, 23-25, 28,29
X	WO 94 19307 A (VOGELBUSCH GMBH ; SARHADDAR SCHAHROCH (AT); SCHEIBL ANTON (AT); BER) 1 September 1994 see page 1, line 1 - page 2, line 3 see page 10, line 1 - page 12, line 5 see example 7 see claims 1-10 --- -/--	1,3-9, 24,25, 28,29

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

16 March 1998

Date of mailing of the international search report

07/04/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (31-70) 240-2040 Telex 31 651 000 N

Authorized officer

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 358 464 A (SOEHNLEN JOSEPH A) 9 November 1982 see column 4, line 34 - column 5, line 19 see column 12, line 64 - column 13, line 12 see claims 8,9 ---	1,3-6, 8-10,12, 23,29,32
X	US 5 369 122 A (STEINMETZER, W., DE) 29 November 1994 see column 3, line 17 - line 65 see column 4, line 21 - line 33 see claims 9-14 ---	1,3-6, 8-10,12, 24,32,33
P,A	WO 97 11047 A (YISSUM R&D COMPANY OF THE HEBREW UNIVERSITY OF JERUSALEM) 27 March 1997 see page 7, line 12 - page 10, line 29 see page 13, line 16 - line 25 see example 3 ---	1-33
A	PATENT ABSTRACTS OF JAPAN vol. 13, no. 302 (C-616), 12 July 1989 & JP 01 091788 A (SHIMADZU CORP., JP), 11 April 1989, see abstract -----	1,3-6, 29,31

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/17774

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR 2674848 A	09-10-92	NONE	
WO 9419307 A	01-09-94	AT 398982 B AT 31093 A DE 59404477 D EP 0684941 A FI 953883 A US 5641406 A	27-02-95 15-07-94 04-12-97 06-12-95 11-09-95 24-06-97
US 4358464 A	09-11-82	NONE	
US 5369122 A	29-11-94	EP 0505596 A DE 59105327 D	30-09-92 01-06-95
WO 9711047 A	27-03-97	AU 6888896 A	09-04-97

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
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Crystal Plaza 2
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ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 18 June 1998 (18.06.98)	
International application No. PCT/US97/17774	Applicant's or agent's file reference 119,389
International filing date (day/month/year) 02 October 1997 (02.10.97)	Priority date (day/month/year) 09 October 1996 (09.10.96)
Applicant EYAL, Aharon, Meir et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
07 May 1998 (07.05.98)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer S. Cruz
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 119,389	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)	
International application No. PCT/US97/17774	International filing date (day/month/year) 02/10/1997	Priority date (day/month/year) 09/10/1996
International Patent Classification (IPC) or national classification and IPC C07C51/47		
Applicant CARGILL INCORPORATED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 07/05/1998	Date of completion of this report 07. 12. 98
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Jardon Alvarez, J Telephone No. (+49-89) 2399-8325 

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. None of the documents cited in the Search Report discloses a process for the recovery of lactic acid from aqueous solutions containing a water-soluble lactate salt using a cation exchanger wherein for the regeneration of the cation exchanger it is converted into a cation exchanger which is at least partially in its acid form and to a second product which is **basic** as described in independent claims 1 and 34.

Accordingly the subject-matter of the claims is novel (Art. 33(2) PCT).

2. The subject-matter of the claims is also based on an inventive step (Art. 33(3) PCT).

As acknowledged at pages 1 to 4 of the present description, processes for the recovery of lactic acid from aqueous solutions are already well known.

The problem to be solved by the present application with respect to said prior art can then be seen as to provide a further process for the recovery of lactic acid. This problem is solved by the process according to claims 1 and 34 which allows a good recovery of lactic acid (see examples).

Although cation exchangers have already been used for the recovery of lactic acid from aqueous solutions containing lactate salts (see, for instance WO - 94/19307 (D1, claims and pages 10 - 12 and examples 5 - 8) and FR - 2 674 848 (D2, claims and examples)) in these known processes the cation exchanger is regenerated with a strong acid to form a salt cation. One would expect that a cation exchanger strong enough for efficient acidulation would be too strong to allow converting the cation-carrying form into the regenerated acid cation exchanger and a basic product. The claimed process which combines efficient acidulation, while still forming a basic product that can be reused as a neutralizing agent is not suggested in the available documents. For these reasons, the subject-matter of the claims is regarded as inventive.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US97/17774

Re Item VI

Certain documents cited (Rule 70.10 PCT)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO - 97/11047	27.03.97	09.09.96	19.09.95

Re Item VIII

Certain observations on the international application

1. Claim 34 that relates to a particular embodiment of the process according to claim 1 should have been appropriately formulated as a claim dependent on claim 1 (Rule 6.4. PCT).
2. The description is not in conformity with the claims as required by Rule 5.1(a)(iii) PCT.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US97/17774

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1,3-16	as originally filed		
2	as received on	09/11/1998 with letter of	05/11/1998

Claims, No.:

19-25	as originally filed		
1-18,26-34	as received on	09/11/1998 with letter of	05/11/1998

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-34
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-34
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-34
	No:	Claims	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US97/17774

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

strongly acidic environment, lactic acid fermentation is conducted at about neutral pH and a neutralizing agent is added for pH adjustment. As the pKa of lactic acid is 3.86, at the pH of fermentation, practically only lactate salts exist. Thus, recovery of lactic acid (in an acid form) from the fermentation liquor requires chemical conversion. Several processes were developed for such conversion.

In some of the processes the conversion liberates lactic acid in solution, e.g. by displacement with a strong acid. Thus, when calcium bases are used as the neutralizing agents in the fermentation, calcium lactate is formed. Reacting the calcium lactate-containing fermentation liquor with sulfuric acid results in precipitation of gypsum and liberation of lactic acid in the solution.

Nakanishi and Tsuda (JP 46/30176) consider production of 1-butyl lactate by extraction of an acidified crude fermentation broth with 1-butanol, followed by esterification of the extract phase. BASF (EP 159-285) considers a similar process with isobutanol to form isobutyl lactate. The process of WO 93/00440, assigned to DU PONT, comprises the steps of: (1) simultaneously mixing a strong acid, an alcohol, and a concentrated fermentation broth which contains mainly basic salts of lactic acid, which react to form a crystal precipitate comprising basic salts of the strong acid and an impure lactate ester of the alcohol; (2) removing water from the mixture as a water/alcohol azeotrope which can be accomplished either sequentially or substantially simultaneously with step (1); removing the crystal precipitate from the mixture; and (4) distilling the impure lactate ester to remove impurities, and recovering the high purity ester.

WHAT IS CLAIMED IS:

1. A process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of:
 - a) contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from said cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from said aqueous solution are bound by said cation exchanger;
 - b) reacting said cations carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cation of said salt; and
 - c) recovering lactic acid from said lactic acid-containing acidulated aqueous solution by methods known per se.
2. A process according to claim 1, wherein said cation exchanger is a liquid cation exchanger.
3. A process according to claim 1, wherein said cation exchanger is a solid cation exchanger.
4. A process according to claim 1, wherein said reaction in said step (b) is a decomposition reaction.

5. A process according to claim 1, wherein said lactic acid is recovered from said lactic acid-containing acidulated aqueous solution simultaneously with the acidulation thereof.
6. A process according to claim 1, wherein said lactic acid is recovered from said lactic acid-containing acidulated aqueous solution after the acidulation of said solution.
7. A process according to claim 1, wherein said second product is used as a neutralizing agent in fermentation.
8. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with a lactic acid extractant.
9. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with a lactic acid absorbent.
10. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with an anion exchanger which is at least partially in its free base form, which anion exchanger is water immiscible in both base and salt form.
11. A process according to claim 1, wherein said anion exchanger is a liquid anion exchanger.

12. A process according to claim 1, wherein said anion exchanger is a solid anion exchanger.

13. A process according to claim 1, wherein said anion exchanger, in its free base form has an apparent basicity corresponding to pKa of not higher than 6.

14. A process according to claim 1, wherein said anion exchanger, in its free base form has an apparent basicity corresponding to pKa of not higher than 4.5.

15. A process according to claim 10, wherein said cation exchanger in its at least partially acid form and said anion exchanger in its at least partially free base form are simultaneously contacted with said lactic acid salt-containing aqueous solution.

16. A process according to claim 10, wherein said cation exchanger in its at least partially acid form and said anion exchanger in its at least partially free base form are repeatedly alternately contacted with said lactic acid salt-containing aqueous solution.

17. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by an anion exchange membrane.

18. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by a dense neutral hydrophilic membrane.

19. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by a dense neutral hydrophobic membrane.

20. A process according to claim 1, wherein said cation exchanger is separated from said aqueous solution by a cation exchange membrane.

21. A process according to claim 1, wherein said cation exchanger is separated from said aqueous solution by a dense neutral hydrophilic membrane.

22. A process according to claim 1, wherein said cation exchanger is separated from said aqueous solution by a dense neutral hydrophobic membrane.

23. A process according to claim 1, wherein said cation exchanger, in its free acid form, has an apparent acidity corresponding to a pK_a of not lower than 2.

24. A process according to claim 4, wherein said decomposition of said cation exchanger salt is by hydrolysis to form the cation exchanger in its at least partially acid form and the second product is a base of the cation forming the salt.

25. A process according to claim 24, wherein said base is selected from the group consisting of ammonia and hydroxides, carbonates and bicarbonates of alkali and alkaline earth metals.

26. A process according to claim 24, wherein hydrolysis is conducted at a temperature higher than 80°C.
27. A process according to claim 4, wherein said second decomposition product is transferred into a vapor phase.
28. A process according to claim 4, wherein said lactic acid salt is ammonium lactate and said second decomposition product is ammonia.
29. A process according to claim 1, wherein said lactate salt is a product of fermentation.
30. A process according to claim 1, wherein the reaction of step b is conducted in a CO₂ containing atmosphere.
31. A process according to claim 1, wherein recovery of lactic acid from said acidulated aqueous solution is effected by distillation.
32. A process according to claim 10, wherein said lactic acid is recovered from said anion exchanger.
33. A process according to claim 1, wherein recovery of lactic acid from said acidulated aqueous solution is effected by distillation of its ester.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EPO

U012120-1

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty.

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND	
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference 119,389	
International application No. PCT/US97/17774	International filing date (day/month/year) 02 October 1997 (02.10.97)	(Earliest) Priority date (day/month/year) 09 October 1996 (09.10.96)	
Title of invention A PROCESS FOR THE RECOVERY OF LACTIC ACID			
Box No. II APPLICANT(S)			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) CARGILL INCORPORATED 15407 McGinty Road West Wayzata, MN 55391-2399 United States of America		Telephone No.:	
		Facsimile No.:	
		Teleprinter No.:	
State (i.e. country) of nationality: United States of America		State (i.e. country) of residence: United States of America	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) EYAL, Aharon Meir 32 Baitar Street Jerusalem 93380 Israel			
State (i.e. country) of nationality: Israel		State (i.e. country) of residence: Israel	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) ELANKOVAN, Ponnampalam 2365 Club Meridian Drive Okemos, MI 48864 United States of America			
State (i.e. country) of nationality: United States of America		State (i.e. country) of residence: United States of America	
<input type="checkbox"/> Further applicants are indicated on a continuation sheet.			

EE 78 4.1 03425US

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCEThe following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

GALLOWAY, Peter D.
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Facsimile No.:

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Teleprinter No.:

☐ Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV STATEMENT CONCERNING AMENDMENTS**

The applicant wishes the International Preliminary Examining Authority*

(i) ☒ to start the international preliminary examination on the basis of the international application as originally filed.(ii) ☐ to take into account the amendments under Article 34 of☐ the description (amendments attached).☐ the claims (amendments attached).☐ the drawings (amendments attached).(iii) ☐ to take into account any amendments of the claims under Article 19 filed with the International Bureau (a copy is attached).(iv) ☐ to disregard any amendments of the claims made under Article 19 and to consider them as reversed.(v) ☐ to postpone the start of the international preliminary examination until the expiration of 20 months from the priority date unless that Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Box No. V ELECTION OF STATES☒ The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)* except

.....

(If the applicant does not wish to elect certain eligible States, the name(s) or country code(s) of those States must be indicated above.)

Box No. VI CHECK LIST

The demand is accompanied by the following documents for the purposes of international preliminary examination:

- | | | |
|--|---|--------|
| 1. amendments under Article 34 | | |
| description | : | sheets |
| claims | : | sheets |
| drawings | : | sheets |
| 2. letter accompanying amendments under Article 34 | : | sheets |
| 3. copy of amendments under Article 19 | : | sheets |
| 4. copy of statement under Article 19 | : | sheets |
| 5. other (specify): | : | sheets |

For International Preliminary
Examining Authority use only

received not received

<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- | | |
|--|--|
| 1. <input type="checkbox"/> separate signed power of attorney | 4. <input checked="" type="checkbox"/> fee calculation sheet |
| 2. <input type="checkbox"/> copy of general power of attorney | 5. <input type="checkbox"/> other (specify): |
| 3. <input type="checkbox"/> statement explaining lack of signature | |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

*Peter D. Galloway by
Joseph H. Handelwa*

PETER D. GALLOWAY
AGENT FOR APPLICANTS

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

- | | |
|--|---|
| 3. <input type="checkbox"/> The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. | <input type="checkbox"/> The applicant has been informed accordingly. |
| 4. <input type="checkbox"/> The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5. | |
| 5. <input type="checkbox"/> Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82. | |

For International Bureau use only

Demand received from IPEA on:

PCT

CHAPTER II

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No. PCT/US97/17774	For International Preliminary Examining Authority use only	
Applicant's or agent's file reference 119,389	Date stamp of the IPEA	
Applicant <div style="text-align: center; font-weight: bold;">CARGILL INCORPORATED, et al.</div>		
Calculation of prescribed fees		
1. Preliminary examination fee	DM 3000.	P
2. Handling fee <i>(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)</i>	DM 285.	H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	<div style="border: 1px solid black; padding: 5px; display: inline-block;"> DM 3285. </div>	
<div style="border: 1px solid black; padding: 2px; display: inline-block;"> TOTAL </div>		
Mode of Payment		
<input checked="" type="checkbox"/> authorization to charge deposit account with the IPEA (see below)	<input type="checkbox"/> cash	
<input type="checkbox"/> cheque	<input type="checkbox"/> revenue stamps	
<input type="checkbox"/> postal money order	<input type="checkbox"/> coupons	
<input type="checkbox"/> bank draft	<input type="checkbox"/> other (specify):	
Deposit Account Authorization <i>(this mode of payment may not be available at all IPEAs)</i>		
The IPEA/ <u>EP</u> <input checked="" type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account.		
<input type="checkbox"/> <i>(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)</i> is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.		
<u>28000092</u> Deposit Account Number	<u>07 May 1998 (07.05.98)</u> Date (day/month/year)	<div style="text-align: center;"> Signature John Richards </div>

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GALLOWAY, Peter D.
LADAS & PARRY
26 West 61st Street
NEW YORK, NY 10023-7604
ETATS-UNIS D'AMERIQUE

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day/month/year)

1 0. 07. 98

Applicant's or agent's file reference

119,389

REPLY DUE

within 3 month(s)
from the above date of mailing

International application no.

PCT/US97/17774

International filing date (day/month/year)

02/10/1997

Priority date (day/month/year)

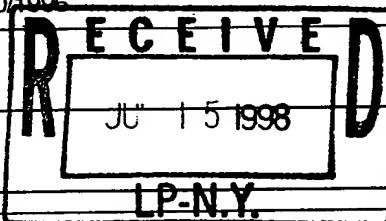
09/10/1996

International Patent Classification (IPC) or both national classification and IPC

C07C51/47

Applicant

CARGILL INCORPORATED et al.



1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and / or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 09/02/1999

Name and mailing address of the international preliminary examining authority

 European Patent Office
D-80298 Munich
Tel. (+49-89) 2399-0, Tx: 523656 epmu d
Fax: (+49-89) 2399-4465

Authorized officer / Examiner

Jardon Alvarez, J

Formalities officer (incl. extension of time limits)

ENTERED BY
Telephone No. (+49-89) 2399-8031

ACTION



**WRITTEN OPINION
SEPARATE SHEET**

International application No. PCT/US97/17774

(D1) WO - 94/19307
(D2) FR - 2 674 848

Re Item V

1. The use of solid cation exchangers for the recovery of lactic acid from aqueous solutions containing lactate salts is already known.
 - 1.1. Thus D1 discloses a process for the recovery of lactic acid wherein in a first step the salt of lactic acid is converted into free acid by means of an ion exchanger in a preliminary column (see page 10, lines 6 -9). The resin used is a cation exchanger, preferably a weakly acid cation exchanger in H⁺ form, which is then regenerated with a diluted strong mineral acid (see page 11, lines 7 - 10 and page 11, line 29 - page 12, line 2). The lactic acid is recovered of the acidulated solution by chromatography in one or more separation columns (page 10, lines 10 - 14). Examples 5 - 8 show the recovery of lactic acid starting from a feed solution at pH 5.8.
 - 1.2. A further process for the separation of lactic acid using solid cation exchangers is disclosed in D2 (see claims and examples).

These disclosures are considered to anticipate the subject-matter of the independent claim 1 which is therefore not novel (Art. 33(2) PCT).

2. Dependent claims 2 to 33 do not appear to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

Re Item VI

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO - 97/11047	27.03.97	09.09.96	19.09.95

**WRITTEN OPINION
SEPARATE SHEET**

International application No. PCT/US97/17774

Re Item VII

1. Claims 11 to 14 should not refer back to the process according to claim 1 because in claim 1 no "anion exchanger" is used (Article 6 PCT).
2. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.
3. The EP citation on the last paragraph of page 2 appears to be wrong and should be checked. It should probably read EP - 0 159 585.

WRITTEN OPINION

International application No. PCT/US97/17774

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-16 as originally filed

Claims, No.:

1-33 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-33
Inventive step (IS)	Claims	1-33
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

November 5, 1998

Facsimile: (49-89) 2399-4465

Confirmation by Courier

International Preliminary Examining Authority
European Patent Office
D-80298 Munich

Dear Sirs:

Re: Cargill Incorporated et al
PCT/US97/17774
International Filing Date: October 2, 1997
Case 119,389

RESPONSE UNDER RULE 66.3 TO WRITTEN OPINION

In response to the Written Opinion issued by the International Preliminary Examining Authority (EPO) on July 10, 1998, applicants present an amended set of claims which distinguish the present invention from the disclosures in WO-94/19307 (D1) and FR-2 674 848 (D2).

This amended set of claims includes an amended claim 1 and an added independent claim, claim 34. The submission of these new claims has entailed the retyping of pages 17, 18, 19 and 21 of the published specification and copies of these new claim pages are enclosed. Additionally, page 2 of the specification is replaced by new page 2 which correctly identifies the prior BASF specification. Again, copies of new page 2 accompany this response.

The Written Opinion also called for reference D1 and D2 to be mentioned in the description. However, it is submitted that these references have little bearing on the invention as defined, and that the prior art documents already acknowledged in the opening paragraphs of the description more properly define the background art. In this connection, it is agreed that the Examiner is correct in taking the position that acidulation of lactate salt with a cation exchanger is obvious. It is submitted that this agreement with the Examiner, or admission of known features, makes it unnecessary even to dwell on the content of references D1 and D2.

The ability of carrying out this process efficiently with a cation exchanger that allows step (b) is not obvious. One would expect that a cation exchanger strong enough for efficient acidulation would be too strong to allow converting the cation-carrying form into the regenerated acid cation exchanger and a basic product. The usual practice, in that case, is regeneration with a strong acid (as indicated by the Examiner), to form a salt of the cation. This salt would represent loss of acid and base and, in many cases, added cost for disposal of a waste stream. The combination of efficient acidulation, while still forming a basic product that can be reused as a neutralizing agent is attractive and is neither taught nor suggested by the cited references.

It is submitted that the foregoing observation substantiates that claim 1, as filed, does indeed define a novel and non-obvious invention. However, with a view to further clarifying the invention claimed in claim 1, that claim has been amplified, in clause (a), to recite that cations from the aqueous solution are bound by the cation exchanger to form a cations-carrying cation exchanger.

New claim 34 is a essentially combination of originally filed claims 1 and 5.

Finally, the dependency of claims 11 to 14 have been corrected.

Respectfully submitted,

Peter D. Galloway

PDG/cgt

strongly acidic environment, lactic acid fermentation is conducted at about neutral pH and a neutralizing agent is added for pH adjustment. As the pKa of lactic acid is 3.86, at the pH of fermentation, practically only lactate salts exist. Thus, recovery of lactic acid (in an acid form) from the fermentation liquor requires chemical conversion. Several processes were developed for such conversion.

In some of the processes the conversion liberates lactic acid in solution, e.g. by displacement with a strong acid. Thus, when calcium bases are used as the neutralizing agents in the fermentation, calcium lactate is formed. Reacting the calcium lactate-containing fermentation liquor with sulfuric acid results in precipitation of gypsum and liberation of lactic acid in the solution.

Nakanishi and Tsuda (JP 46/30176) consider production of 1-butyl lactate by extraction of an acidified crude fermentation broth with 1-butanol, followed by esterification of the extract phase. BASF (EP-0159 585) considers a similar process with isobutanol to form isobutyl lactate. The process of WO 93/00440, assigned to DU PONT, comprises the steps of: (1) simultaneously mixing a strong acid, an alcohol, and a concentrated fermentation broth which contains mainly basic salts of lactic acid, which react to form a crystal precipitate comprising basic salts of the strong acid and an impure lactate ester of the alcohol; (2) removing water from the mixture as a water/alcohol azeotrop which can be accomplished either sequentially or substantially simultaneously with step (1); removing the crystal precipitate from the mixture; and (4) distilling the impure lactate ester to remove impurities, and recovering the high purity ester.

WHAT IS CLAIMED IS:

1. A process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of;
 - a) contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from said cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from said aqueous solution are bound by said cation exchanger to form a cations carrying cation exchanger;
 - b) reacting said cations carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cation of said salt; and
 - c) recovering lactic acid from said lactic acid-containing acidulated aqueous solution by methods known per se.
2. A process according to claim 1, wherein said cation exchanger is a liquid cation exchanger.
3. A process according to claim 1, wherein said cation exchanger is a solid cation exchanger.
4. A process according to claim 1, wherein said reaction in said step (b) is a decomposition reaction.

5. A process according to claim 1, wherein said lactic acid is recovered from said lactic acid-containing acidulated aqueous solution simultaneously with the acidulation thereof.
6. A process according to claim 1, wherein said lactic acid is recovered from said lactic acid-containing acidulated aqueous solution after the acidulation of said solution.
7. A process according to claim 1, wherein said second product is used as a neutralizing agent in fermentation.
8. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with a lactic acid extractant.
9. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with a lactic acid absorbent.
10. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with an anion exchanger which is at least partially in its free base form, which anion exchanger is water immiscible in both base and salt form.
11. A process according to claim 10 wherein said anion exchanger is a liquid anion exchanger.

12. A process according to claim 10, wherein said anion exchanger is a solid anion exchanger.

13. A process according to claim 10, wherein said anion exchanger, in its free base form has an apparent basicity corresponding to pKa of not higher than 6.

14. A process according to claim 10, wherein said anion exchanger, in its free base form has an apparent basicity corresponding to pKa of not higher than 4.5.

15. A process according to claim 10, wherein said cation exchanger in its at least partially acid form and said anion exchanger in its at least partially free base form are simultaneously contacted with said lactic acid salt-containing aqueous solution.

16. A process according to claim 10, wherein said cation exchanger in its at least partially acid form and said anion exchanger in its at least partially free base form are repeatedly alternately contacted with said lactic acid salt-containing aqueous solution.

17. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by an anion exchange membrane.

18. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by a dense neutral hydrophilic membrane.

26. A process according to claim 24, wherein hydrolysis is conducted at a temperature higher than 80°C.
27. A process according to claim 4, wherein said second decomposition product is transferred into a vapor phase.
28. A process according to claim 4, wherein said lactic acid salt is ammonium lactate and said second decomposition product is ammonia.
29. A process according to claim 1, wherein said lactate salt is a product of fermentation.
30. A process according to claim 1, wherein the reaction of step (b) is conducted in a CO₂ containing atmosphere.
31. A process according to claim 1, wherein recovery of lactic acid from said acidulated aqueous solution is effected by distillation.
32. A process according to claim 10, wherein said lactic acid is recovered from said anion exchanger.
33. A process according to claim 1, wherein recovery of lactic acid from said acidulated aqueous solution is effected by distillation of its ester.
34. A process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of;
 - a) contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from said cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from said aqueous solution are bound by said cation exchanger to form a cations-carrying cation exchanger;
 - b) simultaneously recovering lactic acid from said lactic acid-containing acidulated aqueous solution by methods known per se; and
 - c) reacting said cations-carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cations of said salt.

PCI

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

U 012130-1
For Receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) 119,389

Box No. I TITLE OF INVENTION

A PROCESS FOR THE RECOVERY OF LACTIC ACID

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

CARGILL INCORPORATED
15407 McGinty Road West
Wayzata, MN 55391-2399
United States of America

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (i.e. country) of nationality:

United States of America

State (i.e. country) of residence:

United States of America

This person is applicant for the purposes of:

☐

all designated States

☒

all designated States except the United States of America

☐

the United States of America only

☐

the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

EYAL, Aharon Meir
32 Baitar Street
Jerusalem 93380
Israel

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

Israel

State (i.e. country) of residence:

Israel

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☒

the United States of America only

☐

the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒

agent

☐

common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

GALLOWAY, Peter D.
Ladas & Parry
26 West 61st Street
New York, New York 10023
United States of America

Telephone No.

212-708-1905

Facsimile No.

212-2468959

Teleprinter No.

☐ Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> ELANKOVAN, Ponnampalam 2365 Club Meridian Drive Okemos, MI 48864 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State (i.e. country) of nationality: United States of America	State (i.e. country) of residence: United States of America	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> 		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State (i.e. country) of nationality:	State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> 		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State (i.e. country) of nationality:	State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> 		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State (i.e. country) of nationality:	State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box		
<input type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet.		

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☒ AP ARIPO Patent: GH Ghana, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakhstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |
| <input checked="" type="checkbox"/> LS Lesotho | |
| <input checked="" type="checkbox"/> LT Lithuania | |
| <input checked="" type="checkbox"/> LU Luxembourg | |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

☒ ID Indonesia

- ☐
- ☐
- ☐
- ☐

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Supplemental Box *If the Supplemental Box is not used, this sheet need not be included in the request.*

Use this box in the following cases:

1. If, in any of the Boxes, the space is insufficient to furnish all the information:

in particular:

- (i) *if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available:*
- (ii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked:*
- (iii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:*
- (iv) *if, in addition to the agent(s) indicated in Box No. IV, there are further agents:*
- (v) *if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "Continuation" or "Continuation-in-part":*
- (vi) *if there are more than three earlier applications whose priority is claimed:*

in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient;

in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below:

in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;

in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;

in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;

in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;

in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.

2. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty:

in such case, write "Statement Concerning Non-Prejudicial Disclosures or Exceptions to Lack of Novelty" and furnish that statement below.

CONTINUATION OF BOX IV.

WEST, Paul B.
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Box No. VI PRIORITY CLAIMFurther priority claims are indicated in the Supplemental Box ☐

The priority of the following earlier application(s) is hereby claimed:

Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) Israel	09 October 1996 (09.10.96)	119,389	
item (2)			
item (3)			

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

☐ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):
Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA / EPO

Earlier search Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:

Country (or regional Office):

Date (day/month/year):

Number:

Box No. VIII CHECK LIST

This international application contains the following number of sheets:

1. request : 5 sheets
 2. description : 16 sheets
 3. claims : 5 sheets
 4. abstract : 1 sheets
 5. drawings : sheets

Total : 27 sheets

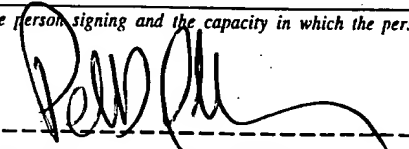
This international application is accompanied by the item(s) marked below:

1. ☐ separate signed power of attorney
 2. ☐ copy of general power of attorney
 3. ☐ statement explaining lack of signature
 4. ☒ priority document(s) identified in Box No. VI as item(s):
 5. ☒ fee calculation sheet
 6. ☐ separate indications concerning deposited microorganisms
 7. ☐ nucleotide and/or amino acid sequence listing (diskette)
 8. ☒ other (specify): Transmittal Letter

Figure No. _____ of the drawings (if any) should accompany the abstract when it is published.

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).


 PETER D. GALLOWAY
 AGENT FOR APPLICANTS

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority specified by the applicant: ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid

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Date of receipt of the record copy by the International Bureau:

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's
file reference

119.389

Applicant

CARGILL INCORPORATED, et al.

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE 240. T

2. SEARCH FEE 1310. S

International search to be carried out by European Patent Office
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

INTERNATIONAL FEE

Basic Fee

The international application contains 27 sheets.

first 30 sheets 530. b₁

x = b₂

remaining sheets additional amount

Add amounts entered at b₁ and b₂ and enter total at B 530. B

Designation Fees

The international application contains 72 designations.

11 x 128. = 1408. D

number of designation fees amount of designation fee
payable (maximum 11)

Add amounts entered at B and D and enter total at I 1938. I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT P

5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P, and enter total in the TOTAL box 3488.
TOTAL

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☐ authorization to charge
deposit account (see below)

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☐ is hereby authorized to charge the total fees indicated above to my deposit account.

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12-0425

02 October 1997 (02.10.97)

Deposit Account Number

Date (day/month/year)

Signature Peter D. Galloway

Case 119,389

SUPPLEMENTARY INFORMATION

With two inventors, an Israeli citizen living in Israel and a US citizen living in the United States, it is not currently known where the invention was conceived, and reduced to practice. This matter is being investigated and a licence is requested as a precaution.

PATENT COOPERATION TREATY

U 012130-1

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

GALLOWAY, Peter, D.
Ladas & Parry
26 West 61st Street
New York, NY 10023
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

16 April 1998 (16.04.98)

Applicant's or agent's file reference

119,389

IMPORTANT NOTICE

International application No.

PCT/US97/17774

International filing date (day/month/year)

02 October 1997 (02.10.97)

Priority date (day/month/year)

09 October 1996 (09.10.96)

Applicant

CARGILL INCORPORATED et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,BR,CA,CN,EP,JP,KP,KR,NO,PL,SK,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
AL,AM,AP,AT,AZ,BA,BB,BG,BY,CH,CU,CZ,DE,DK,EA,EE,ES,FI,GB,GE,GH,HU,ID,IS,KE,KG,KZ,
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UA,UG,UZ,VN,YU,ZW
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
16 April 1998 (16.04.98) under No. WO 98/15518

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶: C07C 51/00	A2	(11) International Publication Number: WO 98/15518 (43) International Publication Date: 16 April 1998 (16.04.98)
(21) International Application Number: PCT/US97/17774 (22) International Filing Date: 2 October 1997 (02.10.97) (30) Priority Data: 119,389 9 October 1996 (09.10.96) IL (71) Applicant (for all designated States except US): CARGILL INCORPORATED [US/US]; 15407 McGinty Road West, Wayzata, MN 55391-2399 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): EYAL, Aharon, Meir [IL/IL]; 32 Baitar Street, 93380 Jerusalem (IL). ELANKOVAN, Ponnampalam [US/US]; 2365 Club Meridian Drive, Okemos, MI 48864 (US). (74) Agents: GALLOWAY, Peter, D.; Ladas & Parry, 26 West 61st Street, New York, NY 10023 (US) et al.		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: A PROCESS FOR THE RECOVERY OF LACTIC ACID		
(57) Abstract <p>The invention provides a process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of: contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from the cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from the aqueous solution are bound by the cation exchanger; reacting the cations carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cation of the salt; and recovering lactic acid from the lactic acid-containing acidulated aqueous solution by methods known per se.</p>		

A PROCESS FOR THE RECOVERY OF LACTIC ACID

The present invention relates to a process for the recovery of lactic acid.

More particularly, the present invention relates to a process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14.

Lactic acid has long been used as a food additive and in various chemical and pharmaceutical applications. More recently, lactic acid has been used in the making of biodegradable polylactic acid polymers as a replacement for present plastic materials, as well as for various new uses where biodegradability is need or desired. Accordingly, there is an ever-increasing demand for lactic acid. The present invention aims at meeting this demand by providing an efficient and environmentally friendly process for producing lactic acid which avoids the consumption of bases and acids and substantially reduces, if not eliminates, the formation of waste or byproduct salts.

The production of lactic acid is commonly carried out by fermentation of a strain of the bacterial genus *lactobacillus delbrueckii* or *Lactobacillus acidophilus*. In general, the production of lactic acid by fermentation in a fermentation broth is well known in the art. The fermentation substrate consists of carbohydrates together with suitable mineral and proteinaceous nutrients. Because the lactic acid-producing microorganisms are inhibited in a

strongly acidic environment, lactic acid fermentation is conducted at about neutral pH and a neutralizing agent is added for pH adjustment. As the pKa of lactic acid is 3.86, at the pH of fermentation, practically only lactate salts exist. Thus, recovery of lactic acid (in an acid form) from the fermentation liquor requires chemical conversion. Several processes were developed for such conversion.

In some of the processes the conversion liberates lactic acid in solution, e.g. by displacement with a strong acid. Thus, when calcium bases are used as the neutralizing agents in the fermentation, calcium lactate is formed. Reacting the calcium lactate-containing fermentation liquor with sulfuric acid results in precipitation of gypsum and liberation of lactic acid in the solution.

Nakanishi and Tsuda (JP 46/30176) consider production of 1-butyl lactate by extraction of an acidified crude fermentation broth with 1-butanol, followed by esterification of the extract phase. BASF (EP-0159 585) considers a similar process with isobutanol to form isobutyl lactate. The process of WO 93/00440, assigned to DU PONT, comprises the steps of: (1) simultaneously mixing a strong acid, an alcohol, and a concentrated fermentation broth which contains mainly basic salts of lactic acid, which react to form a crystal precipitate comprising basic salts of the strong acid and an impure lactate ester of the alcohol; (2) removing water from the mixture as a water/alcohol azeotrop which can be accomplished either sequentially or substantially simultaneously with step (1); removing the crystal precipitate from the mixture; and (4) distilling the impure lactate ester to remove impurities, and recovering the high purity ester.

Alternatively to purifying the lactic acid, which is liberated by displacement with a strong acid, through esterification and distillation of the ester, one could purify it by extraction. The extractant could be a relatively weak one and would allow the recovery of the extracted HLa at high concentration by back-extraction. The known (and food approved) weak extractants to be considered are amine-based ones or solvating extractants (one may consider esters, ethers, ketones, aldehydes, etc., but alkanols seem preferable).

Out of these two groups, the amine-based ones are more attractive for several reasons: (i) they are more selective and would therefore provide for higher product purity, (ii) their extraction capacity is higher and therefore the extractant flow will be lower, and (iii) the amine-based extractants show the temperature sensitivity of the extraction and therefore provide for the "uphill pumping" through back-extraction, at a temperature which is higher than that of the extraction.

These preferred amine-based extractants would not work in a simple process, where the (stronger than lactic) displacing acid is added to the lactate salt-containing solution and the liberated HLa is directly extracted by contact with the extractant. The amine-based extractant prefers the stronger acid in a mixture and would therefore reverse the reaction (remove the added acid).

Acidulating neutral fermentation liquors by the addition of acids usually results in the formation of by-product salts such as the gypsum ammonium and sodium sulfate. Reagents are consumed and disposal of undesired by-products is required.

Efforts have recently been made to recover lactic acid from fermentation liquors without the formation of such by-products. (Such processes will be referred to in the following as salt splitting processes.) In some recently published patents, liquid liquid extraction (LLE) is applied for salt splitting. Thus, in King's US 5,132,456, a strongly basic extractant extracts part of the lactic acid from the neutral solution, which results in a lactic acid loaded extractant and a basic solution. This basic solution, which still contains most of the lactic acid values, could be recycled as a neutralizing medium to the fermentation. In Baniel's US 5,510,526, the extraction of the acid is conducted under CO₂ pressure so that a bicarbonate is formed. The latter can be used as a neutralizing agent in the fermentation. In order to limit the CO₂ pressure to an economic one and still achieve high yields, the extractant used should be quite strong. Recovery of the extracted lactic acid from such strong extractants is difficult, as they hold strongly to it. Recovery of the extracted acid by washing with an aqueous solution of a base is feasible, but forms the lactate salt of the base. It is therefore not practical in those cases where lactic acid is the desired product. Back-extraction with water forms an overly diluted product.

US 5,132,456 suggests a way for recovering extracted carboxylic acid from a strong extractant. It comprises leaching or back-extraction with an aqueous solution of ammonia or low molecular weight alkyl amine, especially trimethyl amine (TMA). The resultant aqueous ammonium or alkylammonium carboxylate solution can be concentrated, if necessary, and the carboxylate can be decomposed thermally to yield the product carboxylic acid and ammonia or amine which can be condensed and recycled. This process is costly and complex. According to the invention, it is particularly problematic

for recovery of extracted lactic acid: "For lactic acid the decomposition is incomplete, being stopped by the formation of a viscous, almost glassy mass containing polymerized lactic acid along with substantial TMA and water. There are, however, effective ways of driving the decomposition to completion for lactic acid, such as diluting the viscous mass with an appropriate solvent (e.g. methyl isobutyl ketone) and continuing the heating and decomposition process."

With these state of the art in mind there is now provided, according to the present invention a process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of: a) contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from said cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from said aqueous solution are bound by said cation exchanger; b) reacting said cations carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cation of said salt; and c) recovering lactic acid from said lactic acid-containing acidulated aqueous solution by methods known per se.

As will be realized in accordance with the present invention, said cation exchanger can be a liquid or solid cation exchanger.

Thus, on contacting the lactate salt-containing solution with the cation exchanger in its acid form an ion exchange is effected. Protons from the

cation exchanger transfer into the aqueous solution where they bind with the lactate anions to form lactic acid. The cations of the lactate salt transfer at the same time to the cation exchanger and transform it into its salt form.

Solid cation exchangers carrying functional groups such as carboxyl or sulfone of the kind used, for example, for de-ionizing solutions, are suitable for the process. So are water-immiscible extractants such as fatty acids, alpha- or beta-halo carboxylic acids, sulfonic acids and mono- or di-esters of phosphoric acid. The cation exchanger salts formed are water immiscible as well, so that, unlike in the case of acidulating by a mineral acid, no salt is added to the broth. The cation exchanger in the acid form needs to be regenerated and is therefore preferably of a weak to medium acidity. It was found that in certain cases highly efficient acidulation is achievable by use of cation exchangers which are significantly weaker acids than lactic acid.

The acid/base properties of water soluble acids or bases are easily determined by their degree of dissociation in aqueous solution. The acid/base properties of water immiscible compounds are determined indirectly through their interaction with solutes in an aqueous solution. Thus the apparent acidity of various liquid or solid cation exchangers can be compared by contacting them with aqueous solutions of NaCl and determining the pH of the aqueous solution in equilibrium. The lower the pH, the stronger the apparent acidity of the cation exchanger. For comparing cation exchangers of relatively low acidity, equilibration with base solutions is preferred. Analogously, the basicity of water immiscible anion exchangers is determined by equilibration with aqueous solutions of salts or acids. Unlike in the case of water soluble acids and bases, the apparent acid/base properties found for water immiscible compounds are determined in addition to the intrinsic

properties of the anion/cation exchanger, by the method of measurement, by phenomena such as steric hindrance, and by the medium (in the case of liquid exchangers).

The salt form of the water immiscible cation exchanger can readily be treated to convert it back to its acid form. This can be achieved by contact with a solution of an acid or an acidic salt, preferably one that is stronger than the cation exchanger. Operating this way consumes a strong acid and could therefore be considered as an indirect acidulation of the lactate salt via a water immiscible cation exchanger. Unlike in the case of direct acidulation by adding a water soluble acid, no salt is formed in the aqueous solution in the case of indirect acidulation and one can use the preferred amine base extractants for the recovery of the liberated acid. Yet an acid is consumed and a by-product salt is formed. There are various ways to split this by-product salt. For example, an acidic ammonium salt of a di- or triprotic acid, e.g., NH_4HSO_4 , could be used as the regenerant of the cation exchanger in an ammonium form. The resulting ammonium sulfate decomposes thermally to ammonia to be reused, and to ammonium bisulfate, which is the acidulant. As long as the lactate is an ammonium lactate the regenerant could be NaHSO_4 or any other acidic sulfate salt, MHSO_4 , which is easy to work with. A metal M that forms MNH_4SO_4 of relatively low solubility is preferable, as it lowers the energy costs related to water evaporation during the thermal decomposition of the salt.

In a preferred embodiment the salt of the cation exchanger is decomposed to reform the acid form and a second product which is basic. An example is the case where the lactate salt is ammonium lactate and an ammonium salt of the water immiscible cation exchanger is formed. The latter

can be decomposed thermally to the cation exchanger in its acid form and to ammonia. Conducting the thermal decomposition at sub-atmospheric conditions or by transfer of a carrier gas helps in shifting the reaction in the desired direction. Steam and CO_2 are among the suitable carrier gases. Compared to the possibility of decomposition of a salt formed on regenerating of the acid form of the cation exchanger by an aqueous solution of an acid, direct decomposition saves on energy consumption for water evaporation. In addition, for a liquid cation exchanger, the decomposition can be assisted by changing the medium/solvent of the salt prior to its decomposition. An alternative to distillation of the second product is the precipitation thereof. Thus, thermal hydrolysis of calcium salts of the cation exchanger forms calcium hydroxide, or if conducted in the presence of CO_2 , CaCO_3 . The crystallization energy of these compounds assists the salt decomposition.

In a further preferred embodiment the second product is basic and can be reused as a neutralizing agent in fermentation. Thus, the lactate salt-containing aqueous solution could be a fermentation broth after removal of the biomass and possibly also after some additional pretreatments. Alternatively, it could be a stream obtained on recovery of lactic acid from broth treated by other methods. If ammonia is used for pH adjustment in the fermentation (i.e. used as the neutralizing agent there), the lactate salt in the broth will be primarily ammonium lactate. Acidulation by water immiscible cation exchanger would convert the latter from its acid form to its ammonium salt. Thermal decomposition of that ammonium salt reforms the cation exchanger in its acid form and forms a second product, ammonia which is basic. In fact the neutralizing agent is regenerated and can be reused in the fermentation. Thereby, the process avoids the consumption of stoichiometric amounts of a neutralizing base and of an acidulant and the formation of a

stoichiometric amount of a by-product salt. Examples for other basic, second decomposition products suitable for reuse in adjusting the pH in fermentation are calcium hydroxide or carbonate and sodium hydroxide, bicarbonate or carbonate resulting from applying the process to calcium lactate or sodium lactate-containing solutions respectively.

The lactic acid in the aqueous phase resulting from the acidulation by the water immiscible cation exchanger is mostly in its free, non-dissociated form. The aqueous solution still comprises most of the impurities it had prior to the acidulation and purification of the lactic acid may be required. That can be effected by one of the very well known methods for purifying lactic acid, including distilling the acid or an ester thereof, adsorption on a solid anion exchanger and solvent extraction. Suitable extractants are solvents such as alkanols, esters, ketones, etc., or extractants comprising water immiscible amines as the main active components. The latter are also considered liquid anion exchangers. Out of these two groups, the amine-based ones are more attractive for several reasons: (i) they are more selective and would therefore provide for higher product purity, (ii) their extraction capacity is higher and therefore the extractant flow will be lower, and (iii) the amine-based extractants show the temperature sensitivity of the extraction and therefore provide for the "uphill pumping" through back-extraction at a temperature which is higher than that of the extraction.

Suitable amines are primary, secondary or tertiary amines with a total carbon atom number of at least 18. Their concentration in the extractant is preferably above 0.5 mole/Kg and more preferably between 0.7 and 1.5 mole/Kg. The upper limit is determined by the viscosity and therefore dependent on the lactic acid concentration in the lactic acid-loaded extractant

(extract) and on the temperature. The diluent for the amine can comprise a variety of solvents such as kerosene, esters, ketones, aldehydes, ethers, alkanols, etc. Polar solvents enhance the extraction efficiency of the extractant due to their effect on the apparent basicity (and are therefore referred to as enhancers). The apparent basicity of the extractant can be increased by 1 to 2 pKa units by adding a suitable enhancer in an amount equivalent to more than 1 mole of enhancer to 1 mole of the amine in the extractant.

Unlike in the cases of salt splitting according to US 5,132,456, US 5,510,526 and others, where no acidulant is added, or where the acidulant is, in fact, a very weak acid, CO₂, the extractant or the anion exchanger in the present invention can be a relatively weak one. Weaker extractants or anion exchangers provide for easier recovery of the separated lactic acid. That is particularly important when the lactic acid is recovered from the extractant or from the water immiscible anion exchanger by back-extraction or by desorption with water. The weaker the extractant or the anion exchanger, the more concentrated will the aqueous product of the back-extraction (back-extract) or desorption (eluate) be. Thus, in the case of extraction by an amine-based extractant, tertiary amines are preferred over primary and secondary amines, and the enhancer content is preferably relatively low. The preferred apparent basicity of the extractant or the anion exchanger is less than 6 and more preferably less than 4.5. Alternatively, in an amine-based extractant the enhancer content in the extraction step is quite high so that the apparent basicity is higher and some of the enhancer is removed from the extract prior to the back-extraction.

Recovery of the lactic acid can be effected after the acidulation and possibly also after the separation of the water immiscible cation exchanger. Alternatively, the recovery of the lactic acid is conducted simultaneously with the acidulation so that both the water immiscible cation exchanger in its acid form and the water immiscible anion exchanger in its free base form are contacted with the lactic acid-containing solution. There are several known arrangements that allow such simultaneous contacting. In one of them the contact is effected in a unit which comprises at least two compartments. In one compartment a liquid cation exchanger is mixed with the lactate salt-containing aqueous solution, while the liquid anion exchanger is situated in or flowing through the other compartment. The two compartments are separated by a membrane that blocks transport of organic phase through it. There is no need to block water or cations. The membrane should let lactic acid through. Most anion exchange membranes and dense neutral hydrophilic membranes are suitable.

Alternatively, one compartment comprises a liquid cation exchanger and the other comprises a mixture of the lactate salt solution and a liquid anion exchanger. In that case the membrane between the compartments could be a cation exchange membrane or a dense neutral hydrophilic one. In a third option there are at least three compartments through which three streams are flowing: (i) the liquid cation exchanger, (ii) the lactate salt-containing aqueous solution, and (iii) the liquid anion exchanger. (i) and (ii) are separated by a cation exchange membrane or a dense neutral hydrophilic membrane, while (ii) and (iii) are separated by an anion exchange membrane (of the type that blocks cations, but allows protons through), or a dense neutral hydrophilic membrane. In some of these embodiments a solid cation

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exchanger could replace the liquid cation exchanger and/or a solid anion exchanger can replace the liquid anion exchanger.

Alternatively to a simultaneous contact with both the cation exchanger and the anion exchanger, the lactate salt-containing solution could be recycled between the two. Thus, it can be contacted with the cation exchanger for partial acidulation, then contacted with the anion exchanger for recovery of some of the free acid, then recycled to the contact with the cation exchanger and so on.

Operating the acidulation by the cation exchanger separately from the recovery of the lactic acid results in a build-up of lactic acid in the aqueous solution. This build-up hinders further acidulation, and in order to reach a nearly complete acidulation, the acidity of the cation exchanger should be similar to or higher than that of lactic acid. Simultaneous contact with, or recycle between, a cation exchanger and an anion exchanger provides for removal of the lactic acid formed on the acidulation and thereby avoids the build-up of the acid in the aqueous solution. As a result, one can use a cation exchanger with a low apparent acidity, lower than that of lactic acid. In this case the decomposition of the salt form of the cation exchanger into the cation exchanger in the acid form and a second basic product is easier.

While the invention will now be described in connection with certain preferred embodiments in the following examples so that aspects thereof may be more fully understood and appreciated, it is not intended to limit the invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalents as may be included within the scope of the invention as defined by the appended claims. Thus,

the following examples which include preferred embodiments will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purposes of illustrative discussion of preferred embodiments of the present invention only and are presented in the cause of providing what is believed to be the most useful and readily understood description of formulation procedures as well as of the principles and conceptual aspects of the invention.

Example 1

Aqueous solutions containing 30% ammonium lactate (initial pH=5.85) are equilibrated at ambient temperature with di-(2-ethyl hexyl) phosphoric acid (DEHPA) at various organic to aqueous ratios. The pH values of the resulting aqueous phase are determined: they are 4.9, 4.1 and 3.2 for organic to aqueous wt/wt ratios of 0.5:1, 1:1 and 3:1 respectively.

In a similar experiment 30% ammonium lactate solutions are contacted with dinonyl naphthalene sulfonic acid (obtained from King Industries as 50% solution in Norpar 12). The pH of the aqueous solutions in equilibrium are 5.1 and 4.5 for organic to aqueous wt/wt ratios of 0.5:1 and 1:1 respectively.

Lowering the pH in contact with the water immiscible cation exchangers is a result of removing ammonium cations from the solution through binding to the cation exchangers and thereby forming lactic acid in said aqueous solution.

Example 2

12.0g aqueous solution containing 0.49 mol/Kg sodium lactate (total of 5.9 mmol lactate) is contacted in a beaker with 1.09g dry cation exchanger Dowex 50x in its acid form (cation exchange capacity of 4.6 equivalent per gram dry). After shaking at ambient temperature for 2 hours, the solution was separated and analyzed for lactic acid by titration. 3.3 equivalents were found indicating conversion of 56% of the sodium lactate to lactic acid through cation exchange.

Example 3.

18.8 aqueous solution containing 2.4 mol/Kg ammonium lactate is equilibrated with 32.6g DEHPA at ambient temperature. An aqueous solution containing 0.97 mol/Kg lactic acid and ammonia containing organic phase are obtained. The organic phase is heated for 2 hours while nitrogen is bubbled through it. Most of its cation exchange capacity is thereby restored. Ammonia is condensed from the vapor phase. 12.3g of the lactic acid containing aqueous phase is equilibrated at ambient temperature with 47g extractant containing 48 wt% tricaprylyl amine (Henkel's Alamine 336), 30% octanol and 22% kerosene. 97% of the lactic acid values in the aqueous phase are extracted into the organic phase. Back-extraction with water at 140°C transfers more than 90% of the extracted acid into the obtained aqueous solution.

Example 4.

The following experiment tested simultaneous contacting of the lactic acid salt-containing aqueous solution with a liquid cation exchanger and a liquid anion exchanger. A three-compartment unit was used. Through one of the compartments a liquid cation exchanger was transferred. This compartment was separated by a membrane from the middle compartment, through which an aqueous solution of lactate salt was flowing. This compartment was separated by a second membrane from a third compartment through which a liquid anion exchanger was transferred. The volumes of the compartments were 10, 5 and 10 ml, respectively. The volumes of all three solutions flowing between their compartments and reservoirs were 100 ml. The flow rates for all three solutions were 50 ml/min. The membranes' working areas were 10^2 cm.

The cation exchanger used was 1.2 mol/kg solution of DEHPA in kerosene. The anion exchanger was a solution containing 1.2 mol/kg Alamine 336 + 20% octanol in kerosene. The aqueous solutions were of 1.0 mol/kg sodium or ammonium lactate. The membranes situated between the cation exchanger and the aqueous solution were Neosepta CM-1 or CM-2 cation exchange membranes obtained from Tokayama Soda Co. Those situated between the aqueous solution and the anion exchanger were Neosepta ACH-45 or Neosepta AFX, both are anion exchange membranes obtained from Tokayama Soda Co, or Celgard 3400, a dense hydrophilic membrane obtained from Celanese Co.

The rates of cations transport into the cation exchanger and of the simultaneous transport of lactic acid into the anion exchanger were followed. The flow rates in all the combinations tested were typically higher than $3 \cdot 10^{-5}$ mol/m² sec.

It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrative examples and that the present invention may be embodied in other specific forms without departing from the essential attributes thereof, and it is therefore desired that the present embodiments and examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

WHAT IS CLAIMED IS:

1. A process for the recovery of lactic acid from aqueous solutions containing at least one water-soluble lactate salt and having a pH of about between 4 and 14, comprising the steps of:

a) contacting said aqueous solution with a cation exchanger which is at least partially in its acid form, said cation exchanger being water immiscible in both acid and salt form, whereby ion exchange is effected, protons are transferred from said cation exchanger to the aqueous solution to acidulate it and to form lactic acid therein and cations from said aqueous solution are bound by said cation exchanger;

b) reacting said cations carrying cation exchanger to convert it into a cation exchanger which is at least partially in its acid form and to a second product, which second product is basic and comprises the cation of said salt; and

c) recovering lactic acid from said lactic acid-containing acidulated aqueous solution by methods known per se.

2. A process according to claim 1, wherein said cation exchanger is a liquid cation exchanger.

3. A process according to claim 1, wherein said cation exchanger is a solid cation exchanger.

4. A process according to claim 1, wherein said reaction in said step (b) is a decomposition reaction.

5. A process according to claim 1, wherein said lactic acid is recovered from said lactic acid-containing acidulated aqueous solution simultaneously with the acidulation thereof.
6. A process according to claim 1, wherein said lactic acid is recovered from said lactic acid-containing acidulated aqueous solution after the acidulation of said solution.
7. A process according to claim 1, wherein said second product is used as a neutralizing agent in fermentation.
8. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with a lactic acid extractant.
9. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with a lactic acid absorbent.
10. A process according to claim 1, wherein said recovery of said lactic acid from the acidulated aqueous solution is effected by contacting said solution with an anion exchanger which is at least partially in its free base form, which anion exchanger is water immiscible in both base and salt form.
11. A process according to claim 1, wherein said anion exchanger is a liquid anion exchanger.

12. A process according to claim 1, wherein said anion exchanger is a solid anion exchanger.
13. A process according to claim 1, wherein said anion exchanger, in its free base form has an apparent basicity corresponding to pKa of not higher than 6.
14. A process according to claim 1, wherein said anion exchanger, in its free base form has an apparent basicity corresponding to pKa of not higher than 4.5.
15. A process according to claim 10, wherein said cation exchanger in its at least partially acid form and said anion exchanger in its at least partially free base form are simultaneously contacted with said lactic acid salt-containing aqueous solution.
16. A process according to claim 10, wherein said cation exchanger in its at least partially acid form and said anion exchanger in its at least partially free base form are repeatedly alternately contacted with said lactic acid salt-containing aqueous solution.
17. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by an anion exchange membrane.
18. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by a dense neutral hydrophilic membrane.

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26. A process according to claim 24, wherein hydrolysis is conducted at a temperature higher than 80°C.
27. A process according to claim 4, wherein said second decomposition product is transferred into a vapor phase.
28. A process according to claim 4, wherein said lactic acid salt is ammonium lactate and said second decomposition product is ammonia.
29. A process according to claim 1, wherein said lactate salt is a product of fermentation.
30. A process according to claim 1, wherein the reaction of step b is conducted in a CO₂ containing atmosphere.
31. A process according to claim 1, wherein recovery of lactic acid from said acidulated aqueous solution is effected by distillation.
32. A process according to claim 10, wherein said lactic acid is recovered from said anion exchanger.
33. A process according to claim 1, wherein recovery of lactic acid from said acidulated aqueous solution is effected by distillation of its ester.

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19. A process according to claim 10, wherein said anion exchanger is separated from said aqueous solution by a dense neutral hydrophobic membrane.

20. A process according to claim 1, wherein said cation exchanger is separated from said aqueous solution by a cation exchange membrane.

21. A process according to claim 1, wherein said cation exchanger is separated from said aqueous solution by a dense neutral hydrophilic membrane.

22. A process according to claim 1, wherein said cation exchanger is separated from said aqueous solution by a dense neutral hydrophobic membrane.

23. A process according to claim 1, wherein said cation exchanger, in its free acid form, has an apparent acidity corresponding to a pK_a of not lower than 2.

24. A process according to claim 4, wherein said decomposition of said cation exchanger salt is by hydrolysis to form the cation exchanger in its at least partially acid form and the second product is a base of the cation forming the salt.

25. A process according to claim 24, wherein said base is selected from the group consisting of ammonia and hydroxides, carbonates and bicarbonates of alkali and alkaline earth metals.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 119,389	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 97/ 17774	International filing date (day/month/year) 02/10/1997	(Earliest) Priority Date (day/month/year) 09/10/1996
Applicant CARGILL INCORPORATED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).
2. ☐ Unity of invention is lacking (see Box II).
3. ☐ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
 - ☐ filed with the international application.
 - ☐ furnished by the applicant separately from the international application,
 - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - ☐ Transcribed by this Authority

4. With regard to the **title**,
 - ☐ the text is approved as submitted by the applicant
 - ☒ the text has been established by this Authority to read as follows:

A PROCESS FOR THE RECOVERY OF LACTIC ACID FROM AQUEOUS LACTATE SALT SOLUTIONS, INVOLVING THE USE OF ION EXCHANGERS

5. With regard to the **abstract**,
 - ☒ the text is approved as submitted by the applicant
 - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

Figure No. —

 - ☐ as suggested by the applicant.
 - ☐ because the applicant failed to suggest a figure.
 - ☐ because this figure better characterizes the invention.
 - ☐ None of the figures.

INTERNATIONAL SEARCH REPORT *

International Application No

PCT/US 97/17774

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07C51/47 C07C51/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 2 674 848 A (SOCIETE ANGEVINE DE BIOTECHNOLOGIE BIOPROX, FR) 9 October 1992 see page 1, line 1 - page 2, line 17 see example 2 ---	1,3-6, 23-25, 28,29
X	WO 94 19307 A (VOGELBUSCH GMBH ; SARHADDAR SCHAHROCH (AT); SCHEIBL ANTON (AT); BER) 1 September 1994 see page 1, line 1 - page 2, line 3 see page 10, line 1 - page 12, line 5 see example 7 see claims 1-10 --- -/--	1,3-9, 24,25, 28,29



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

16 March 1998

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 97/17774

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 4 358 464 A (SOEHNLEN JOSEPH A) 9 November 1982</p> <p>see column 4, line 34 - column 5, line 19 see column 12, line 64 - column 13, line 12 see claims 8,9</p> <p style="text-align: center;">---</p>	<p>1,3-6, 8-10,12, 23,29,32</p>
X	<p>US 5 369 122 A (STEINMETZER, W., DE) 29 November 1994</p> <p>see column 3, line 17 - line 65 see column 4, line 21 - line 33 see claims 9-14</p> <p style="text-align: center;">---</p>	<p>1,3-6, 8-10,12, 24,32,33</p>
P,A	<p>WO 97 11047 A (YISSUM R&D COMPANY OF THE HEBREW UNIVERSITY OF JERUSALEM) 27 March 1997</p> <p>see page 7, line 12 - page 10, line 29 see page 13, line 16 - line 25 see example 3</p> <p style="text-align: center;">---</p>	<p>1-33</p>
A	<p>PATENT ABSTRACTS OF JAPAN vol. 13, no. 302 (C-616), 12 July 1989 & JP 01 091788 A (SHIMADZU CORP., JP), 11 April 1989, see abstract</p> <p style="text-align: center;">-----</p>	<p>1,3-6, 29,31</p>

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Information on patent family members

International Application No

PCT/US 97/17774

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